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SUMMARY MINUTES

OF THE

EAR, NOSE AND THROAT DEVICES

ADVISORY PANEL MEETING

OPEN SESSION

**June 18, 1999
9200 Corporate Blvd.
Conference Room 020 B
Rockville, MD 20850**

**Ear, Nose and Throat Devices Panel Roster
June 18, 1999**

Carl A. **Patow**, M.D., MPH
Chair

Harry R. Sauberman
Acting Executive Secretary

Emmett E. Campbell, M.D.
Voting Member

William H. **Duffell**, Ph.D.
Industry Representative

Anjum Khan, M.D.
Voting Member

Paul R. Kileny, Ph.D.
Voting Member

Renee Middleton, Ph.D.
Consumer Representative

Clough Shelton, M.D.
Voting Member

Yvonne S. Sininger, Ph.D.
Voting Member

Peter Uhthoff, M.D.
Invited Guest

Gayle E. **Woodson**, M.D.
Voting Member

FDA Participants

A. Ralph Rosenthal, M.D.
Director, Division of Ophthalmic Devices

Dr. Sid Jaffee

Teri Cygnarowicz

June 18, 1999--OPEN SESSION

Dr. Carl A. Patow, Panel Chair, called the Open Session to order at 8:45 a.m., stating that the purpose of the meeting was to discuss, on a generic level, issues of safety and efficacy related to implantable middle ear amplification devices. This information would be used to develop a guidance document for manufacturers to follow when preparing submissions to the agency. He asked members of the panel to introduced themselves. Harry R. Sauberman, Acting Panel Executive Secretary, introduced Dr. Peter Uhthoff, a visiting expert from the Canadian Ministry of Health, noting that the FDA is engaged in a partnering venture with the Ministry in this area.

Dr. Patow reviewed activities at the May 21, 1997, Ear, Nose and Throat Devices Panel Meeting, at which Advanced Bionics presented a premarket advisory (PMA) for a Multi-Strategy Cochlear Implant intended for use with children ages 2 to 17 and with infants with a lower age limit of 18 months diagnosed with an ossified cochlea. The PMA, which received conditional approval from the panel, has now completed the conditions and received marketing approval.

Mr. Sauberman read the conflict of interest statement, noting that matters concerning Drs. Kileny, Sininger, and Shelton had been considered but deemed to pose no conflict of interest.

Thomas Shope of the Division of Electronics and Computer Science at the Office of Science and Technology gave the panel an update on the Year 2000 date problem as it concerns computerized medical devices. He noted that many medical devices are subject to Year 2000 problems: these include microprocessor or personal

computer (PC)-controlled products, medical device software applications, device interfaces to databases and recordkeeping, and embedded chips for date display or recording. Mr. Shope defined the Year 2000 problem and read a definition of Year 2000 compliance, noting that a Year 2000 compliant-product is a product that is impervious to the date change. Mr. Shope requested panel assistance in three areas. These included advice regarding products in members' areas that could be affected, identification of types of products that could present actual patient risks, and suggestions regarding other actions to reduce risks. Advice could be sent to his attention or directed to Acting Panel Executive Secretary, Harry Sauberman.

Mr. Shope summarized **FDA/CDRH** activities on the Year 2000 problem to date. He noted that the FDA has a biomedical equipment database on its World Wide Web site that is continually updated and contains voluntary submission of data provided by manufacturers. The database shows that many companies have not yet reported. Most of the noncompliant products have date stamping problems, which is a less serious issue, but a limited number have operational problems. Manufacturers are providing a variety of solutions. The FDA can require recall of devices presenting a significant risk to public health and will monitor reports of **Y2K** problems with emphasis on devices that could present significant patient risks. Mr. Shope listed future **CDRH/FDA** activities and healthcare facility issues and asked the panel to give the problem serious consideration.

Dr. Tom Gross of the FDA gave the panel a presentation on postmarket surveillance and methods of postmarket evaluation at CDRH. He explained that medical devices have a definable life cycle, in which the clinical community has an important role to play in providing feedback during postmarket evaluation. He outlined the questions

assessed in the postmarket period and described the Medical Device Reporting (MDR) Program, which provides limited but critical information to FDA about devices with problems, and he listed the possible actions prompted by such a medical device report. Dr. Gross discussed the two postmarket authorities, postmarketing surveillance and postapproval authority, and outlined the criteria for a panel to suggest postmarketing surveillance as well as study designs used in postmarketing surveillance. He **acknowledged** the frustrations involved in monitoring the postmarketing period and challenged the advisory panel to ensure that a postmarketing study will be of primary importance, to **specify** the public health question it is to address, and to note what will be done with the data collected. He briefly outlined the future for the MDR and Postmarketing Surveillance programs.

OPEN PUBLIC DISCUSSION

Presentations by Members of the Public

Dr. Michael Glasscock, III, of the University of Tennessee Health Science Center, discussed ethical considerations for implantable hearing devices. He discussed the extent of hearing problems and the reasons why external hearing devices are often not used. Dr. Glasscock analyzed types and technologies of implantable devices, as well as surgical requirements. Saying that ethical considerations include safety and effectiveness; Dr. Glasscock compared fenestration, stapes, endolymphatic shunt procedures, and **cochlear** implant surgeries and also discussed cosmetic considerations and issues of patient choice. He concluded that millions of patients may benefit from implantable hearing devices.

Dr. Lorenz Lassen of the American Academy of Otolaryngology stated that **otolaryngologists** support the continued development and use of surgically implantable electronic hearing devices as an important new option for those who have derived little benefit from conventional hearing aids or are frustrated by them. He summarized some of the more important benefits as improved sound quality and speech intelligibility, elimination of acoustic feedback, improved sound localization, and improved comfort, reliability, and aural hygiene. Safety considerations include the generally known risks of anesthesia and surgery, difficulties with magnetic resonance imaging (MRI), and limited availability of data on long-term effects.

Dr. Sigfrid D. Soli of the House Ear Institute addressed effectiveness issues. He defined efficacy as functional superiority to air conduction aids and discussed both monaural and binaural use. **Dr. Soli** listed the practical limitations of implantable middle ear amplification devices and discussed how effectiveness is achieved **and** demonstrated.

Mr. Henry Ilecki and Ms Evelyn Cherow of the American Speech-Language-Hearing Association recommended that five broad areas of investigation be included during the agency's deliberations: 1) analysis of safety and efficacy of the technology, **from** the perspectives of etiology, type, and degree of hearing loss, other audiometric factors, perceived disability and quality of life, and history of amplification use; 2) compatibility with other amplification and telecommunications technologies; 3) **cost-benefit** analysis; 4) consideration of candidacy criteria; and 5) the essential need for comprehensive pre and post-implant audiological evaluation and treatment.

Brenda Battat of Self-Help for Hard of Hearing People, Inc. listed six concerns related to the safety and efficacy of implantable hearing devices: 1) that

potential candidates should be provided with realistic performance outcomes and a **cost/** benefit ratio should be determined; 2) that appropriate rehabilitation following surgery should ensure comfortable and successful device use; 3) that device **immunity** to electromagnetic interference must be ensured; 4) that the device must be designed to be used with telephones inductively and acoustically; 5) that the device must be designed to allow use with assistive listening devices; and 6) that evidence must attest to medical safety.

Dr. Stanley Baker of the Otologic Medical Center discussed issues related to the surgical procedure, the device, and risks /benefits associated with performing such surgeries on a normal middle ear anatomy. He made the following points:

1. The surgical technique used is an adaptation of the **cochlear** implant procedure.
2. Preservation of the patient's residual hearing is a primary concern.
3. An implant device and procedure that does not structurally alter the middle ear anatomy is desirable.
4. The weight of middle ear implants can have a significant effect on residual hearing by adding mass to the ossicular chain.
5. Adequate postoperative healing should be allowed before device activation.
6. Device configuration should allow for the possibility of revision surgery.
7. Any implantable device and implant surgery should be reversible.
8. Theoretical and real limitations on future MRI scanning should be addressed with each device.
9. The device should not interrupt the blood supply to the ossicles to minimize potential long-term negative effects.

10. A semi-implantable device affords the possibility of upgrades, improvements and technological enhancements as they occur.

OPEN COMMITTEE DISCUSSION

Harry Sauberman, Acting Panel Chair, read the charge to the panel, to discuss issues of safety and **efficacy** for a new application of technology for the hearing impaired known as implantable middle ear amplification devices.

Presentations by Manufacturers

Dr. Jonathan Spindel of the University of Virginia Center for Sensory-Neural Engineering discussed the mechanics of implantable **hearing devices** and their improvements over conventional acoustic transduction. He also presented material on the Round Window Electromagnetic (RWEM) implantable hearing device, which takes an electromagnetic approach using a magnet applied to the round window membrane. Dr. Spindel concluded with a brief description of laser vibrometry methods of evaluating hearing devices.

Dr. Iain L. Grant of St. Croix Medical, Inc., discussed preclinical investigation of an implantable hearing device. After outlining the components of such devices, he discussed the use of freshly harvested cadaver temporal bones and animal models for evaluating implants and compared them to the human model. He concluded that the temporal bone and animal models are complementary, with the former providing reliable performance information and the latter useful for tissue response and toxicity effects.

Mr. Jose Bedoya of Otologics discussed clinical trial design issues, such as the need for a baseline trial using conventional hearing instruments, appropriate outcome assessment measurements, and issues in comparing performance of conventional hearing

aids and implantable middle ear devices. He analyzed surgical and device-related risks in terms of comparisons of surgical procedures and known **complications**, device design issues that affect long-term safety, and reversibility and limitations to normal auditory function. He also looked at criteria for candidate selection and predictability of outcomes and claims. Mr. Bedoya concluded that substantial benefit in patient performance must be demonstrated to justify surgery on a normal middle ear, and it must be demonstrated using a well-controlled comparison. That comparison must include the best acoustic hearing aid fitting possible as a baseline reference condition, the use of comparable baseline and implant fitting and evaluation techniques, and the use of an appropriate and wide range of outcome measurements that are well validated.

Pam Matthews of Soundtec, Inc. presented recommendations for preclinical and clinical design considerations. For the preclinical standard, she recommended the human temporal bone model in conjunction with laser Doppler interferometry. For clinical studies, she gave inclusion criteria of moderate to severe SNHL with the possibility of normal hearing for 1000 HZ and below and a speech score for the NU-6 50 item word lists of 60 % or greater. Feedback, occlusion, or dissatisfaction with an optimally fit hearing aid must be substantiated. The subject would function as his own control, using an optimally fit hearing aid, which she defined as meeting a prescriptive target of NAL-R by plus or minus five decibels for 500-2000 HZ and plus or minus 12 decibels for 3000-4000 HZ, have aided benefit substantiated by validated tool, and pass a hearing aid checklist. In terms of safety, risks must be outweighed by benefits, with some residual hearing loss and loading expected, but the risk of severe hearing loss not to exceed that of a stapedectomy. Efficacy outcomes should include SII, functional gain measures, speech

recognition scores in quiet and noise, substantiation of aided benefit and increased sound quality, decreased occlusion and feedback with validated tools. The power of the study and sensitivity to change of primary outcomes should dictate sample size. For example, her company's model requires approximately 100 subjects studied for **six** months and then postmarket approval surveillance for one year.

Dr. –Ing Hans Leysieffer and Dr. John McElveen of Implex described the Totally Implantable Cochlea Amplifier (**TICA**) device. Dr. Leysieffer discussed general and clinical aspects of the device, technical or audiological aspects, safety considerations, and training and education. Dr. McElveen reviewed the surgical procedure and considerations.

Mr. Michael Crompton, Mr. Bob Katz, and Ms. Deborah Arthur of Symphonix discussed regulatory considerations for an implantable middle ear hearing device (IMEHD). They proposed an IMEHD identification and classification for the panel and outlined its regulatory status in the United States, Canada, and the European Union. They asked the panel to use appropriate and available guidance controls already recognized by the panel such as conformance to design controls for investigational devices and recognition of consensus standards, where appropriate, and to use previous guidelines as a model. They briefly listed design considerations for such devices and described their device, the Vibrant Soundbridge. They recommended that clinical considerations for a guidance document should include use of appropriate selection criteria for presurgical evaluation and should incorporate many of the standard audiological measures adaptable to IMEHDs. Objective measures of immittance audiometry include tympanometry, static immittance, and acoustic reflexes. Behavioral

assessment should include standard audiometric battery at implant and nonimplant ear including air/bone conduction, and speech audiometry. Evaluation of the patient's existing amplification system should include electro-acoustic verification Probe microphone measures of hearing aids and behavioral measures with hearing aids. **Self-**assessment questionnaires provide significant clinical measures of a patient's performance and expectations. The implanting procedures should have no adverse effect upon residual hearing, the patient should receive counseling for realistic expectations, and device placement should be revisable and allow the patient to revert to hearing aid.

Dr. Anthony Maniglia of Case Western Reserve University discussed advantages and disadvantages of semi-implantable electronic hearing devices. He suggested that the advantages of such devices were probably not good enough to compare them to binaural conventional hearing aids with state-of-the-art technology because of cost. He listed acceptable complications and selection criteria for enrollment in a study for semi-implantable devices, but he concluded that future developments and technology are on the side of a totally implantable hearing device, saying that the semi-implantable device will probably be short-lived.

Dr. Sid Jaffee of the FDA briefly reviewed the evolution of middle and inner ear surgery and listed risk to benefit considerations for surgery to correct hearing loss. He and Teri Cygnarowicz read the FDA panel questions for discussion and provided comments on them.

Dr. Clough Shelton of the panel began the discussion of safety questions. In discussing how much benefit justifies performing surgery on a normal middle ear, it was suggested that a detailed list of risks should be available as well as a sense of benefits in

comparison to a baseline or control. In general, the sense of the panel was that if there are hearing benefits, it is worthwhile having surgery on a normal middle ear.

The panel found it not relevant or not useful to compare implantable middle ear device surgery to stapes surgery. The sense of the panel was that the nerve conduction or **cochlear** hearing postoperatively should be the same as the hearing preoperatively, and that labeling for individual devices will be critical because the risks for individual devices differ.

The panel recommended that devices should be MRI-compatible if possible but noted that other methods such as CT scans can be used in place of **MRIs** as long as patients and providers can be adequately warned. Monopolar electrocautery was seen as a potentially more serious issue.

The panel had a number of concerns for possible further impairment of the auditory system over time because of the lack of long-term data. They recommended monaural implantation until such data are available, although some members suggested binaural implantation for patients who have had successful monaural implantation after one year. Concerns included sensoneural degradation, conductive degradation, effect upon the ossicular chain, the need for maximum output cutoff levels, and so forth. Concerns such as **software**, chips, microphone, and battery performance could be answered in the shorter term; one to two years was suggested. Devices that do more damage to the ossicle should present longer follow-up data.

Preclinical data that the panel thought would be most beneficial included maintenance of device integrity over the long term, biocompatibility of new materials in devices, battery replacement issues, and surgical accessibility. Human temporal bone is

the best model to assess adequacy of amplification; animal models are useful for biocompatibility. Laser Doppler vibrometer studies are also useful.

Other points the panel thought should be covered in a guidance document included the possibility for surgical revision because of device failure or upgrading considerations and any possible limitations on physical activity, such as scuba diving. It was suggested that following the guidance document on cochlear implants might be useful in this regard.

Regarding risk versus benefit, the panel suggested that the optimal control would be best aided results for experienced hearing aid users with a one-month trial baseline. An option for manufacturers would be best binaural aids for inexperienced users for three months. Test batteries should include some measure of speech recognition, functional gain, and speech in quiet and noise. It was suggested that manufacturers consider measuring binaural hearing to measure directional hearing and sound localization.

In assessing clinically significant changes in residual hearing, the panel suggested bone conduction tests and speech intelligibility discrimination changes. Air and bone conduction should both be tested. Some patient satisfaction questionnaire or quality of life questionnaire similar to the cochlear implant questionnaire should be used.

The panel appeared somewhat divided about restricting the device to patients demonstrating certain types or degrees of hearing loss. Patients with stable hearing loss showing no increase in hearing loss over a two year period, excluding those with Meniere's disease, was suggested. The range of hearing loss should be related to what the device can hope to achieve; it was recommended that the manufacturer should indicate

use and provide the data. The best or cleanest study would be with moderate hearing loss, with no floor on speech intelligibility necessary.

On measurement of fidelity, the panel recommended using fresh human temporal bone for preclinical bench testing and some subjective psychophysical measure of patient satisfaction. They did not see this issue as related to candidacy criteria.

On binaural versus monaural implantation, the panel suggested monaural implantation should be standard for clinical trials, but binaural implantation should be allowed if acceptable to the patient and results of the initial implant are stable at one year. They also recommended a contraindication against operating on the only hearing ear.

On device accommodation for future hearing changes, it was suggested that devices should have the same range of flexibility of responses as conventional hearing aids. It was suggested that this is a manufacturers' challenge more than a guidance document issue.

Significant Issues of Safety and Efficacy in Development of a Guidance Document

Panel members then had the opportunity to repeat or express new individual concerns on significant issues involving safety and **efficacy** that should be included in the guidance document.

Preclinical concerns expressed included biocompatibility issues and assessment of mechanical performance in the human temporal bone model. Documentation should be done on device durability and integrity on a preclinical basis. Physical activation tests similar to those done with **cochlear** implants should be performed, and the device battery should be easily disconnectable and removable. It was noted that certain devices may require specific animal tests for specific issues.

On clinical design issues, it was noted that the minimum number of patients to be included in a study should be looked at, as should the length of follow-up; guidance recommendations should be soundly based but least burdensome. The target population, type of controls, frequency of follow-up and types of measurement should be outlined in the study protocol. The guidance document should acknowledge that the claims and indications drive the type of study required and that the risks may differ for different types of devices. Use of international standards should be referenced and specified. One member recommended that clinical studies not be limited to moderate to severe hearing loss and that the studies not be limited to monaural implantation; monaural versus binaural implantation would depend on the length of development of the device.

The guidance document should specify what the minimal criteria and baseline data would be for effectiveness. Patients should be characterized on speech stimuli and pure tone discrimination as compared to unaided hearing and optimized with best fitted conventional hearing aids. Efficacy should be measured by comparison to best aided speech, but unaided speech should be evaluated as well. Speech intelligibility function for single words and in noise should be measured. The APHAD test should be used, and subjective measures such as assessment and patient self-reporting should be done pre and post implantation. Any quality of life instrument should be validated in the intended use population.

Safety concerns involved placement of the device over the ossicle, the range of movement in this area, and the failure rate in this location; effects of device removal on ear structure; surgeon competency and training issues, especially using the facial recess approach; and the need for prevention of microphone feedback. Information should be

provided on long-term risks for coupling to the structures of the middle ear.

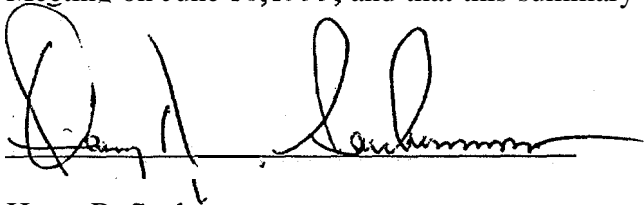
Documentation should be done on surgical variability for devices with direct coupling to the ossicular chain. A patient identification bracelet should be used to warn about use of **MRI** or electrocautery in patients implanted with the device, to prevent risks to patients who are unconscious or unable to communicate.

Panel members suggested that training and testing tools and information should be provided in the labeling but certification by sponsors should not be required.

Specialized training, especially in surgical **technique**, was emphasized.

Panel Chair Dr. **Patow** thanked the panel, FDA, industry, and individual speakers for their input and noted that there would be further opportunities to provide such input before the guidance document is finalized. The meeting was adjourned at **4:40** p.m.

I **certify** that I attended the Open Session of the Ear, Nose and Throat Devices Panel Meeting on June 18, 1999, and that this summary accurately reflects what transpired.

A handwritten signature in black ink, appearing to read "Harry R. Sauberman", written over a horizontal line.

Harry R. Sauberman
Acting Executive Secretary

I approve the minutes of this meeting as recorded in this summary.

A handwritten signature in black ink, appearing to read "Carl A. Patow", written over a horizontal line.

Carl A. Patow, M.D.
Panel Chair

Summary minutes prepared by

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